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=> file reg COST IN U.S. DOLLARS

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STRUCTURE FILE UPDATES: 2 OCT 2002 HIGHEST RN 458522-67-3 DICTIONARY FILE UPDATES: 2 OCT 2002 HIGHEST RN 458522-67-3

TSCA INFORMATION NOW CURRENT THROUGH MAY 20, 2002

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Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details: http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

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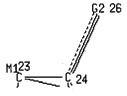
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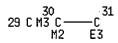
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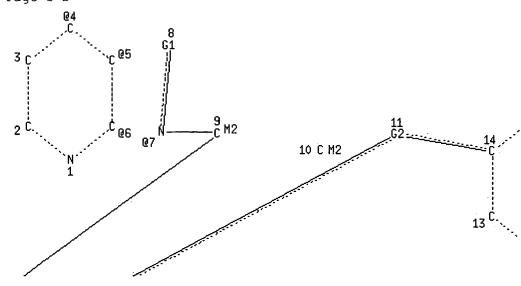


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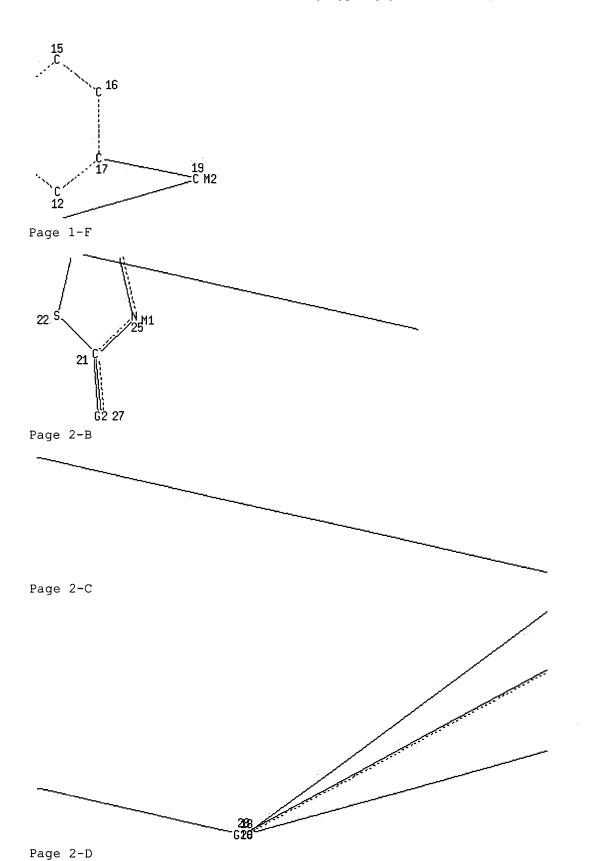
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NUMBER OF NODES IS 33

STEREO ATTRIBUTES: NONE

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100.0% PROCESSED 10 ITERATIONS

2 ANSWERS

SEARCH TIME: 00.00.02

FULL FILE PROJECTIONS: ONLINE **COMPLETE**

BATCH **COMPLETE**

PROJECTED ITERATIONS: 11 TO

PROJECTED ANSWERS:

2 TO 124

389

L2 2 SEA SSS SAM L1

=> s l1 full

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100.0% PROCESSED 310 ITERATIONS

48 ANSWERS

SEARCH TIME: 00.00.06

L3 48 SEA SSS FUL L1

=> file hcaplus

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INCE FILE TOTAL
ENTRY SESSION
143.70 143.91

FULL ESTIMATED COST

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FILE COVERS 1907 - 3 Oct 2002 VOL 137 ISS 14 FILE LAST UPDATED: 2 Oct 2002 (20021002/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

CAS roles have been modified effective December 16, 2001. Please check your SDI profiles to see if they need to be revised. For information on CAS roles, enter $\underline{\text{HELP ROLES}}$ at an arrow prompt or use the CAS Roles thesaurus (/RL field) in this file.

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490 L3

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L5 324 L3/THU

(L3 (L) THU/RL)

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2340863 METHOD 982149 METHODS

3048039 METHOD

(METHOD OR METHODS)

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94540 DIAB?

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53014 MELLIT?

L8 44 L7 AND MELLIT?

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(PD<19990520)

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L9 ANSWER 1 OF 17 HCAPLUS COPYRIGHT 2002 ACS

17 L8 AND PD < MAY 20 1999

Full Citing : Text References

L9

ACCESSION NUMBER: 2000:362595 HCAPLUS

DOCUMENT NUMBER: 133:13403

TITLE: Adipocyte containing ob gene promoter for screening

modulators useful in treatment of anorexia, obesity,

and other diseases

INVENTOR(S):
Briggs, Michael R.; Auwerx, Johan; De Vos, Piet;

Staels, Bart; Croston, Glenn E.; Miller, Stephen G.

PATENT ASSIGNEE(S): Ligand Pharmaceuticals Inc., USA

SOURCE: U.S., 64 pp., Cont.-in-part of U.S. Ser. No. 558,588,

abandoned.

CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO. DATE
US 6068976	Α	20000530	US 1996-618100 19960319
CA 2215387	AA	19960926	CA 1996-2215387 19960319
PRIORITY APPLN. INFO	. :		US 1995-408584 B2 19950320
			US 1995-418096 B2 19950405
			US 1995-510584 B2 19950802
			US 1995-558588 B2 19951030
			US 1995-7390P P 19951121
			US 1995-7721P P 19951130
			US 1995-8601P P 19951214

AB This invention relates to the isolation and cloning of the promoter and other control regions of a human ob gene. It provides a **method** for identifying and screening for agents useful for the treatment of diseases and pathol. conditions affected by the level of expression of an ob gene. These agents interact directly or indirectly with the promoter or other

control regions of the ob gene. A PPARy agonist, BRL49653, has been identified to be useful in treating anorexia, cachexia, and other diseases characterized by insufficient food intake or body wt. loss. Modulators of ob gene expression may be used to treat other diseases such as obesity, diabetes, hypertension, cardiovascular diseases and infertility.

IT 122320-73-4, BRL49653

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(PPARy agonist; adipocyte contg. ob gene promoter for screening modulators useful in treatment of anorexia, obesity, and other diseases)

122320-73-4 HCAPLUS RN

 $\overline{2,4-\text{Thiazol}}$ idinedione, 5-[[4-[2-(methyl-2-pyridinylamino)]] ethoxy] phenyl] met CN hyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

PAGE 2-A



REFERENCE COUNT:

THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 2 OF 17 HCAPLUS COPYRIGHT 2002 ACS

9

Citing Full References

ACCESSION NUMBER: DOCUMENT NUMBER:

1999:316557 HCAPLUS

130:332912

TITLE:

Activators of the nuclear orphan receptor peroxisome proliferator-activated receptor gamma for treatment of

INVENTOR(S):

diabetes and cardiovascular disorders Kliewer, Steven Anthony; Lehmann, Jurgen M.; Willson,

Timothy M.

PATENT ASSIGNEE(S):

SOURCE:

Glaxo Wellcome Inc., USA

U.S., 9 pp., Cont. of U.S. Ser. No. 804,310,

abandoned.

CODEN: USXXAM

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5902726	A	19990511	US 1998-28988	19980225
US 5994554	A	19991130	US 1998-207936	19981209
PRIORITY APPLN.	INFO.:		US 1994-363482	19941223
			US 1995-386394	19950210
			US 1997-804310	19970221
			US 1998-28988	19980225

OTHER SOURCE(S): MARPAT 130:332912

AB The present invention provides activator compds., including agonists, to the peroxisome proliferator-activated receptor gamma. Particular PPARy activators are set forth, as are a pharmaceutical compn. for treating diabetes, non-insulin-dependent diabetes mellitus, cardiovascular disorders, and methods for such treatment. Also claimed is a method of identifying activator compds.

IT 173792-21-7

RL: ARG (Analytical reagent use); THU (Therapeutic use); BSU (Biological study, unclassified); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PROC (Process); USES (Uses) (for identifying PPAR γ -interacting compds. useful as drugs; activators of peroxisome proliferator-activated receptor gamma for treatment of diabetes and cardiovascular disorders)

RN 173792-21-7 HCAPLUS

CN 2,4-Thiazolidinedione, 5-[[4-[2-(methyl-2-pyridinylamino)ethoxy]phenyl]met hyl]-, labeled with tritium (9CI) (CA INDEX NAME)

PAGE 1-A

PAGE 2-A



REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 3 OF 17 HCAPLUS COPYRIGHT 2002 ACS

Full Citing Text References

ACCESSION NUMBER: 1999:167677 HCAPLUS

DOCUMENT NUMBER: 131:124868

TITLE: Systemic exposure to rosiglitazone is unaltered by

food

AUTHOR(S): Freed, M. I.; Allen, A.; Jorkasky, D. K.; DiCicco, R.

Α.

CORPORATE SOURCE: SmithKline Beecham Clinical Pharmacology Unit,

Presbyterian Medical Center of the University of Pennsylvania Health System, 51 North 39th Street,

Philadelphia, PA, 19104, USA

SOURCE: European Journal of Clinical Pharmacology (1999),

55(1), 53-56

CODEN: EJCPAS; ISSN: 0031-6970

PUBLISHER: Springer-Verlag

DOCUMENT TYPE: Journal LANGUAGE: English

AB Objective: To evaluate the effect of food on the bioavailability and pharmacokinetics of the insulin sensitizer rosiglitazone. Methods: In a randomized, open-label, period-balanced, single-dose, crossover study, rosiglitazone 2 mg was administered to 12 healthy male volunteers either in the fasting state or following a std. high-fat breakfast. The primary end points of the study were AUCO-inf and Cmax. Results: Single oral doses of rosiglitazone were safe and well tolerated. Overall exposure to rosiglitazone was unaffected by food. The geometric mean ratio of AUC(0-inf) in the fed:fasted regimens was 0.94 (95% CI: 0.82, 1.06); t1/2was unaffected. Absorption of rosiglitazone in the fed state was more gradual and sustained than in the fasted state. Cmax was reduced by approx. 20% (point est. 0.80; 95% CI 0.65 to 0.97) and tmax was modestly delayed in the fed state. Conclusion: These data support dosing guidelines that will permit the administration of rosiglitazone without regard to meals for treatment of type 2 diabetes mellitus.

IT 122320-73-4, Rosiglitazone

RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

(bioavailability of antidiabetic rosiglitazone is unaltered by food intake in humans)

RN 122320-73-4 HCAPLUS

CN 2,4-Thiazolidinedione, 5-[[4-[2-(methyl-2-pyridinylamino)ethoxy]phenyl]met hyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

PAGE 2-A

REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 4 OF 17 HCAPLUS COPYRIGHT 2002 ACS

Full Citing Text References

ACCESSION NUMBER: 1999:81575 HCAPLUS

DOCUMENT NUMBER: 130:134189

TITLE: Treatment of diabetes with a thiazolidinedione, an

insulin secretagogue, and an α -glucosidase

inhibitor

INVENTOR(S): Buckingham, Robin Edwin; Smith, Stephen Alistair

PATENT ASSIGNEE(S): Smithkline Beecham PLC, UK

SOURCE: PCT Int. Appl., 20 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PAT	rent	NO.		KI	ND	DATE	ATE APPLICATION NO. DATE										
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AB A method and compn. are disclosed for the treatment of diabetes mellitus and conditions assocd. with diabetes mellitus in a mammal. The method comprises administering an effective nontoxic and pharmaceutically acceptable amt. of an insulin sensitizer, an insulin secretagogue and an α -glucosidase inhibitor antihyperglycemic agent to a mammal in need thereof.

IT 122320-73-4

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)

(thiazolidinedione, insulin secretagogue, and $\alpha\text{-glucosidase}$ inhibitor for diabetes treatment)

RN 122320-73-4 HCAPLUS

CN 2,4-Thiazolidinedione, 5-[[4-[2-(methyl-2-pyridinylamino)ethoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

PAGE 2-A

REFERENCE COUNT:

THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 5 OF 17 HCAPLUS COPYRIGHT 2002 ACS

7



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ACCESSION NUMBER:
                         1999:81574 HCAPLUS
                         130:134188
DOCUMENT NUMBER:
TITLE:
                         Treatment of diabetes with a thiazolidinedione, an
                         insulin secretagogue, and a biguanide
INVENTOR(S):
                         Buckingham, Robin Edwin; Smith, Stephen Alistair
PATENT ASSIGNEE(S):
                         Smithkline Beecham PLC, UK
SOURCE:
                         PCT Int. Appl., 19 pp.
                         CODEN: PIXXD2
DOCUMENT TYPE:
                         Patent
LANGUAGE:
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FAMILY ACC. NUM. COUNT:
PATENT INFORMATION:
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                                          APPLICATION NO. DATE
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AΒ
    A method and compn. are disclosed for the treatment of diabetes
    mellitus and conditions assocd. with diabetes mellitus in a mammal.
    The method comprises administering an effective nontoxic and
    pharmaceutically acceptable amt. of an insulin sensitizer, an insulin
     secretagogue and a biguanide antihyperglycemic agent to a mammal in need
    thereof.
IT 122320-73-4
    RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); THU (Therapeutic use); BIOL (Biological
     study); USES (Uses)
        (thiazolidinedione, insulin secretagogue, and biguanide for
        diabetes treatment)
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RN

CN

122320-73-4 HCAPLUS

hyl] - (9CI) (CA INDEX NAME)

2,4-Thiazolidinedione, 5-[[4-[2-(methyl-2-pyridinylamino)ethoxy]phenyl]met

PAGE 1-A

REFERENCE COUNT:

THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 6 OF 17 HCAPLUS COPYRIGHT 2002 ACS

7

Full Citing Text References

ACCESSION NUMBER:

1999:81573 HCAPLUS

DOCUMENT NUMBER: 130:134187

TITLE:

Treatment of diabetes with insulin sensitizer

thiazolidinedione and insulin secretagogue

sulfonylurea

INVENTOR(S):

Buckingham, Robin Edwin; Smith, Stephen Alistair

PATENT ASSIGNEE(S): Smithkline Beecham PLC, UK

SOURCE: PCT

PCT Int. Appl., 19 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PAT	ENT	NO.		KI	ND	DATE			A:	PPLI	CATI	и ис	o.	DATE			
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PRIORITY APPLN. INFO	. :		GB 1997-15306 A	19970718
			WO 1998-GB2109 W	19980716
			US 1999-445907 A1	19991215

AB A method for the treatment of diabetes mellitus and conditions assocd. with diabetes mellitus in a mammal, which method comprises administering an effective non-toxic and pharmaceutically acceptable amt. of an insulin sensitizer and a sub-maximal amt. of an insulin secretagogue, to a mammal in need thereof; and a pharmaceutical compn. for use in such method are disclosed. The insulin secretagogue is esp. sulfonylurea. The insulin sensitizer is esp. 5-[4-[2-(N-methyl-N-(2-pyridyl)amino)ethoxy]benzyl]thiazolidine-2,4-dione (I). Tablet formulations contg. I maleate are given.

IT 122320-73-4

RN

CN

RL: THU (Therapeutic use); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

(as insulin sensitizer; treatment of **diabetes** with insulin sensitizer thiazolidinedione and insulin secretagogue sulfonylurea) 122320-73-4 HCAPLUS

2,4-Thiazolidinedione, 5-[[4-[2-(methyl-2-pyridinylamino)ethoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

PAGE 2-A



8

REFERENCE COUNT:

THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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ANSWER 7 OF 17
                    HCAPLUS COPYRIGHT 2002 ACS
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         References
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                         1999:9712 HCAPLUS
ACCESSION NUMBER:
                         130:61091
DOCUMENT NUMBER:
                         Treatment of diabetes with thiazolidinedione and
TITLE:
                         sulfonylurea
INVENTOR(S):
                         Smith, Stephen Alistair
                         Smithkline Beecham Plc, UK
PATENT ASSIGNEE(S):
SOURCE:
                         PCT Int. Appl., 20 pp.
                         CODEN: PIXXD2
DOCUMENT TYPE:
                         Patent
                         English
LANGUAGE:
FAMILY ACC. NUM. COUNT:
PATENT INFORMATION:
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                                        US 1999-445859
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     A method for the treatment of diabetes mellitus and conditions
AB
     assocd. with diabetes mellitus in a mammal, which method comprises
     administering an effective nontoxic and pharmaceutically acceptable amt.
     of an insulin sensitizer and an insulin secretagogue, to a mammal in need
     thereof.
IT 155141-29-0, Rosiglitazone maleate
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); THU (Therapeutic use); BIOL (Biological
     study); USES (Uses)
        (treatment of diabetes with thiazolidinedione and
        sulfonylurea)
     155141-29-0 HCAPLUS
RN
     2,4-Thiazolidinedione, 5-[[4-[2-(methyl-2-pyridinylamino)ethoxy]phenyl]met
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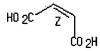
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CM 2

CRN 110-16-7 CMF C4 H4 O4

Double bond geometry as shown.



REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 8 OF 17 HCAPLUS COPYRIGHT 2002 ACS

Full Citing Text References

ACCESSION NUMBER: 1999:9699 HCAPLUS

DOCUMENT NUMBER: 130:61090

TITLE: Treatment of diabetes with rosiglitazone and insulin

INVENTOR(S): Smith, Stephen Alistair

PATENT ASSIGNEE(S): Smithkline Beecham P.L.C., UK

SOURCE: PCT Int. Appl., 17 pp.

CODEN: PIXXD2
DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE

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PRIORITY APPLN. INFO.:
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AB A method for the treatment of diabetes mellitus and conditions assocd. with diabetes mellitus in a mammal, which method comprises administering an effective nontoxic and pharmaceutically acceptable amt. of insulin sensitizer rosiglitazone and insulin to a mammal in need thereof.

IT 155141-29-0, Rosiglitazone maleate

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(treatment of **diabetes mellitus** with rosiglitazone and insulin)

RN <u>155141-29-0</u> HCAPLUS

CN 2,4-Thiazolidinedione, 5-[[4-[2-(methyl-2-pyridinylamino)ethoxy]phenyl]met hyl]-, (2Z)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 122320-73-4 CMF C18 H19 N3 O3 S

PAGE 1-A



CM 2

CRN <u>110-16-7</u> CMF <u>C4 H4 O4</u>

Double bond geometry as shown.

HO 2C Z CO 2H

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 9 OF 17 HCAPLUS COPYRIGHT 2002 ACS

Full Citing Text References

ACCESSION NUMBER: 1999:9698 HCAPLUS

DOCUMENT NUMBER: 130:76189

TITLE: Treatment of **diabetes** with thiazolidinedione and

alpha-glucosidase inhibitor

INVENTOR(S): Smith, Stephen Alistair
PATENT ASSIGNEE(S): Smithkline Beecham Plc, UK
SOURCE: PCT Int. Appl., 19 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

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										WO 1	998-	EP36	<u>91</u>	W	1998	0615		

<u>US 1999-445951</u> B1 19991215 <u>US 2001-863136</u> B1 20010523

GI

AB A method for the treatment of diabetes mellitus and conditions assocd. with diabetes mellitus in a mammal, which method comprises administering an effective non-toxic and pharmaceutically acceptable amt. of an insulin sensitizer (I) and an α -glucosidase inhibitor antihyperglycemic agent. The effects of α -glucosidase inhibitor acarbose on the pharmacokinetics of I in healthy humans are described along with pharmaceutical formulations (concns. and tablets) contg. I.

IT 155141-29-0

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(treatment of diabetes mellitus and conditions assocd. with diabetes with thiazolidinedione deriv. and α -glucosidase inhibitors)

RN 155141-29-0 HCAPLUS

CN 2,4-Thiazolidinedione, 5-[[4-[2-(methyl-2-pyridinylamino)ethoxy]phenyl]met hyl]-, (2Z)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 122320-73-4 CMF C18 H19 N3 O3 S

PAGE 1-A

PAGE 2-A

CM 2

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Double bond geometry as shown.

HO 2C Z CO 2H

REFERENCE COUNT:

7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 10 OF 17 HCAPLUS COPYRIGHT 2002 ACS

Full Citing Text References

ACCESSION NUMBER: 1999:9697 HCAPLUS

DOCUMENT NUMBER: 130:61089

TITLE: Treatment of diabetes with thiazolidinedione and

metformin

INVENTOR(S): Smith, Stephen Alistair
PATENT ASSIGNEE(S): Smithkline Beecham Plc, UK
SOURCE: PCT Int. Appl., 20 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE

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    A method for the treatment and/or prophylaxis of diabetes mellitus,
AB
     conditions assocd. with diabetes mellitus, and certain complications
     thereof, in a mammal which method comprises administering an effective
    nontoxic and pharmaceutically acceptable amt. of an insulin sensitizer
     rosiglitazone (I) and a biguanide antihyperglycemic agent such as
     metformin. Pharmacokinetics of I and metformin administered alone or in
     combination are described. Formulations for prepg. tablets contg. I is
     presented.
IT 155141-29-0, Rosiglitazone maleate
     study, unclassified); THU (Therapeutic use); BIOL (Biological
     study); USES (Uses)
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RL: BAC (Biological activity or effector, except adverse); BSU (Biological

(treatment of diabetes with thiazolidinedione insulin sensitizer and metformin)

RN 155141-29-0 HCAPLUS

2,4-Thiazolidinedione, 5-[[4-[2-(methyl-2-pyridinylamino)ethoxy]phenyl]met CN hyl]-, (2Z)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

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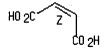
122320-73-4 CRN C18 H19 N3 O3 S CMF



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CRN 110-16-7 C4 H4 O4 CMF

Double bond geometry as shown.



REFERENCE COUNT:

5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 HCAPLUS COPYRIGHT 2002 ACS ANSWER 11 OF 17

Full Text

ACCESSION NUMBER: 1998:764284 HCAPLUS

DOCUMENT NUMBER: 130:10664

TITLE: Use of 5-(4-(2-(N-methyl-N-(2-

pyridyl)amino)ethoxy)benzyl)-2,4-thiazolidinedione in

the treatment of polycystic ovary syndrome and

gestational diabetes

INVENTOR(S): Antonucci, Tammy; Lockwood, Dean; Norris, Rebecca

Warner-Lambert Company, USA PATENT ASSIGNEE(S):

SOURCE: PCT Int. Appl., 55 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT:

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AB Novel methods of using thiazolidinone derivs. and related antihyperglycemic agents to treat populations at risk for developing noninsulin-dependent diabetes mellitus (NIDDM) and complications arising therefrom are disclosed. In one embodiment, the compds. of the invention are used to treat polycystic ovary syndrome to prevent or delay the onset of noninsulin-dependent diabetes mellitus. In another embodiment, the compds. of the invention are used to treat gestational diabetes to prevent or delay the onset of noninsulin-dependent diabetes mellitus.

IT 122320-73-4

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(ste ns treatment of polycystic ovary syndrome and gestational
diabetes and prevention of NIDDM development by
(methyl)pyridyl)

RN 122320-73-4 HCAPLUS

CN 2,4-Thiazolidinedione, 5-[[4-[2-(methyl-2-pyridinylamino)ethoxy]phenyl]met hyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

PAGE 2-A

REFERENCE COUNT:

THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 12 OF 17 HCAPLUS COPYRIGHT 2002 ACS

8

Full Citing Text References

ACCESSION NUMBER:

BER: 1998:672463 HCAPLUS

DOCUMENT NUMBER: 129:270626

TITLE: Methods and compositions for treating and/or

preventing non-insulin dependent diabetes mellitus

(NIDDM) using specific retinoid compounds

INVENTOR(S): Pfahl, Magnus; Lernhardt, Waldemar; Fanjol, Andrea

PATENT ASSIGNEE(S): Centre International de Recherches Dermatologiques

Galderma, Fr.

SOURCE: PCT Int. Appl., 21 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

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JP 2001521551	Т2	20011106	JP 1998-545851 19980324
NO 9904612	A	19991124	NO 1999-4612 19990902
PRIORITY APPLN. INFO	. :		US 1997-35604P P 19970324
			WO 1998-US5591 W 19980324

AB Methods are provided for treating and/or preventing non-insulin dependent diabetes mellitus (NIDDM) in subjects having or at substantial risk of developing NIDDM, using specific retinoid compds. that are structurally related to 9-cis retinoid acid which induce the differentiation of preadipocytes into adipocytes. These compds. may be administered alone or in combination with other anti-diabetogenic agents such as thiazolidinediones.

IT 122320-73-4

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(retinoid compds. with other agents for treating and/or preventing non-insulin dependent diabetes mellitus)

RN 122320-73-4 HCAPLUS

CN 2,4-Thiazolidinedione, 5-[[4-[2-(methyl-2-pyridinylamino)ethoxy]phenyl]met hyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

PAGE 2-A



L9 ANSWER 13 OF 17 HCAPLUS COPYRIGHT 2002 ACS

Full Citing Text References

ACCESSION NUMBER: DOCUMENT NUMBER: TITLE:

1998:41808 HCAPLUS

128:123811

Use of thiazolidinedione derivatives and related

antihyperglycemic agents in the treatment of insulin-resistant subjects with normal glucose tolerance in order to prevent or delay the onset of

noninsulin-dependent diabetes mellitus

INVENTOR(S):
Olefsky, Jerrold M.

PATENT ASSIGNEE(S): Sankyo Company, Limited, Japan

SOURCE: U.S., 16 pp.
CODEN: USXXAM

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

OTHER SOURCE(S):

PATENT NO. KIND DATE APPLICATION NO. DATE
US 5708012 A 19980113 US 1995-431266 19950428

MARPAT 128:123811

AB **Methods** are disclosed for using thiazolidinone derivs. and related antihyperglycemic agents to treat populations exhibiting insulin-resistant non-impaired glucose tolerance in order to prevent or delay the onset of noninsulin-dependent **diabetes mellitus** and complications arising therefrom. In an outpatient trial with nondiabetic, obese patients, some of whom had impaired glucose tolerance, (+)-5-[[4-[(3,4-dihydro-6-hydroxy-2,5,7,8-tetramethyl-2H-1-benzopyran-2-yl)methoxy]phenyl]methyl]-2,4-thiazolidinedione (troglitazone) normalized glucose tolerance and markedly improved insulin resistance and hyperinsulinemia.

IT 122320-73-4

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(thiazolidinedione derivs. and related antihyperglycemic agents in treatment of insulin-resistant subjects with normal glucose tolerance to prevent or delay onset of noninsulin-dependent diabetes

mellitus)

RN 122320-73-4 HCAPLUS

PAGE 1-A



L9 ANSWER 14 OF 17 HCAPLUS COPYRIGHT 2002 ACS

Full Citing Text References

ACCESSION NUMBER: 1997:329275 HCAPLUS

DOCUMENT NUMBER: 126:308792

TITLE: Treating NIDDM with RXR agonists

INVENTOR(S): Heyman, Richard A.; Cesario, Rosemary; Mukherjee,

Ranjan

PATENT ASSIGNEE(S): Ligand Pharmaceuticals Incorporated, USA

SOURCE: PCT Int. Appl., 56 pp.

CODEN: PIXXD2

DOCUMENT TYPE: LANGUAGE: Patent English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

	PAT	CENT	NO.			ND.	DATE			I	APPLI	CATI	ON No	0.	DATE			
	WO	9710	 819				1997	0327		V	70 19	 96-℧	S149	04	1996	0917		
		W:	ES, LU,	FI, LV,	GB, MD,	GE, MG,	HU, MK,	IS, MN,	JP, MW,	KE, MX,	KG, NO,	KP, NZ,	KR, PL,	KZ, PT,	CZ, LK, RO,	LR, RU,	LS, SD,	LT, SE,
				SI, RU,			TM,	TR,	TT,	UA,	UG,	UZ,	VN,	AM,	AZ,	BY,	KG,	KZ,
		RW:													FI, CM,			
	CA	2232	288		A	A.	1997	0327		(:A 19	96-2	2322	88	1996	0917		
	AU	9670	742		A.	1	1997	0409		7	U 19	96-7	0742		1996	0917		
	ΑU	9670 7259	98		В	2	2000	1026		-								
	EP	8596	80		A:	1	1998	0826		E	IP 19	96-9	3161	3	1996	0917		
		R:			CH,	DE,	DK,	ES,	FR,	GB,	GR,	ΙT,	LI,	LU,	NL,	SE,	MC,	PT,
			ΙE,	FΙ														
		9610			A					_	3R 19				1996			
		1151								_				_	1996			
		6028													1996			
		5972						1026		7	JS 19	<u>97-9</u>	7972	<u>5</u>	1997	1126		
		9801	192					0518							1998			
	-	6228						0508		_	JS 19			_	1999			
		6316				1	2001	1113		_				_	2000			
PRIO	RITY	APP	LN.	INFO	. :										1995			
										US I	1995-	4897	<u>P</u>	P	1995	1006		
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7/ 17	መሎ -				mal = 4		+	a - h -							1999		o.f	
AB		ls in									-							or

AB This invention relates to methods and compns. for the treatment of non-insulin-dependent diabetes mellitus using an RXR agonist alone or in combination with a PPARγ agonist such as thiazolidine dione compd. Example RXR agonists are LGD 1069, ALRT 1957 and LG 100268.

IT 122320-73-4, BRL 49653

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (noninsulin dependent diabetes treatment with RXR agonists)

RN <u>1</u>22320-73-4 HCAPLUS

CN $\frac{2}{4}$ -Thiazolidinedione, 5-[[4-[2-(methyl-2-pyridinylamino)ethoxy]phenyl]met

hyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

PAGE 2-A



L9 ANSWER 15 OF 17 HCAPLUS COPYRIGHT 2002 ACS

Full Citing Text References

ACCESSION NUMBER: 1997:231131 HCAPLUS

DOCUMENT NUMBER: 126:207528

TITLE: A thiazolidione derivative for reducing the amount of

exogenous insulin administered to a patient having

noninsulin-dependent diabetes mellitus

INVENTOR(S): Whitcomb, Randall W.

PATENT ASSIGNEE(S): Warner-Lambert Company, USA; Whitcomb, Randall W.

SOURCE: PCT Int. Appl., 43 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT NO.	KIND DATE	APPLICATION NO. DATE
WO 9705875 WO 9705875	A2 1997022 A3 1997032	
W: AU, BG,	CA, CN, CZ, EB	G, GE, HU, IL, JP, KR, LT, LV, MX, NO, NZ,
PL, RO,	SG, SI, SK, UA	, US, UZ, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: AT, BE,	CH, DE, DK, ES	, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE
CA 2221241	AA 1997022	O CA 1996-2221241 19960729
AU 9666411	A1 1997030	5 AU 1996-66411 19960729
AU 724989	B2 2000100	5
EP 851757	A2 1998070	8 EP 1996-926171 19960729
R: AT, BE,	CH, DE, DK, ES	, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,

IE, SI, LT, LV, FI A 19980909 CN 1996-196191 19960729 CN 1192683 T2 JP 1996-508479 19960729 JP 11510508 19990914 NO 1998-556 NO 9800556 19980209 19980209 Α PRIORITY APPLN. INFO.: US 1995-2098P Ρ 19950810 WO 1996-US12430 W 19960729

MARPAT 126:207528 OTHER SOURCE(S): AΒ

This invention provides a method of reducing the amt. of exogenous insulin administered to a patient having noninsulin-dependent diabetes mellitus by administering to a patient a therapeutically effective amt. of a thiazolidione deriv. and/or a related compd. Seventeen patients with noninsulin-dependent diabetes mellitus that were still on insulin were treated with thiazolidinedione deriv. (400 mg/day) for 8 wk. Ten patients have had a mean decrease of 45% (39 units) in their daily dose of insulin and appear to be continuing to reduce their insulin requirements. At the same time, their glycemic control was improving with a mean decrease of 15% (36 mg/dL) in blood glucose. A total of 7 patients have had their insulin discontinued after 8 wk.

IT **122320-73-4**, BRL 49653

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(thiazolidione deriv. and/or related compds. for reducing amt. of exogenous insulin in humans with noninsulin-dependent diabetes mellitus)

122320-73-4 HCAPLUS RN

2,4-Thiazolidinedione, 5-[[4-[2-(methyl-2-pyridinylamino)ethoxy]phenyl]met CN hyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

PAGE 2-A

ANSWER 16 OF 17 HCAPLUS COPYRIGHT 2002 ACS L9



ACCESSION NUMBER: 1996:713048 HCAPLUS

125:319877 DOCUMENT NUMBER:

Adipocyte containing ob gene promoter for screening TITLE:

modulators useful in treatment of anorexia, obesity,

and other diseases

Briggs, Michael R.; Auwerx, Johan; De Vos, Piet; INVENTOR(S):

Staels, Bart; Croston, Glenn E.; Miller, Stephen G.

Ligand Pharmaceuticals Incorporated, USA; Institut PATENT ASSIGNEE(S):

Pasteur De Lille

SOURCE: PCT Int. Appl., 166 pp.

CODEN: PIXXD2

Patent DOCUMENT TYPE: LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PA	TENT I	NO.		KIND DATE APPLICATION						ON NO	o.	DATE					
	9629								W	0 19	96-U	S380	<u>8</u>	1996	0319		
WO	9629																
	W:	AL,	AM,	ΑT,	AU,	ΑZ,	BB,	BG,	BR,	BY,	CA,	CH,	CN,	CZ,	DE,	DK,	EE,
		ES,	FΙ,	GB,	GE,	ΗU,	IS,	JP,	ΚĖ,	KG,	KP,	KR,	ΚZ,	LK,	LR,	LS,	LT,
		LU.	LV.	MD.	MG,	MK,	MN,	MW,	MX,	NO,	NZ,	PL,	PT,	RO,	RU,	SD,	SE,
		SG,		•	•	•	•	•	•	•	•	·	·	•	•	·	•
	RW:			MW.	SD,	SZ.	UG,	AT,	BE.	CH,	DE,	DK,	ES,	FΙ,	FR,	GB,	GR,
														CM,			
CA	2215	•		•				•	•				-	-		•	
	9655																
	8152																
EP																MC	DM
	R:			CH,	DE,	DK,	ES,	FK,	GB,	GK,	IT,	η ι ,	TO,	NL,	SE,	MC,	PI,
		IE,											_				
PRIORIT	<u>Y</u> APP:	LN.	INFO	. :										1995	-		
											<u>4180</u>			1995	0405		
								İ	US 1	995-	5105	84	Α	1995	0802		
								1	US 1	995-	5585	88	Α	1995	1030		
								1	US 1	995-	7390	P	Ρ	1995	1121		
								•	US 1	995-	7721	P	Р	1995	1130		
														1995			
														1996			

AΒ This invention relates to the isolation and cloning of the promoter and other control regions of a human ob gene. It provides a method for identifying and screening for agents useful for the treatment of diseases and pathol. conditions affected by the level of expression of an ob gene. These agents interact directly or indirectly with the promoter or other control regions of the ob gene. A PPARy agonist, BRL49653, has been identified to be useful in treating anorexia, cachexia, and other diseases characterized by insufficient food intake or body wt. loss. Modulators of ob gene expression may be used to treat other diseases such as obesity, diabetes, hypertension, cardiovascular diseases and infertility.

IT **122320-73-4**, BRL49653

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(PPARy agonist; adipocyte contg. ob gene promoter for screening modulators useful in treatment of anorexia, obesity, and other diseases)

RN 122320-73-4 HCAPLUS

2,4-Thiazolidinedione, 5-[[4-[2-(methyl-2-pyridinylamino)ethoxy]phenyl]met CN hyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

L9 ANSWER 17 OF 17 HCAPLUS COPYRIGHT 2002 ACS

Full Citing Text References

ACCESSION NUMBER: 1996:71475 HCAPLUS

DOCUMENT NUMBER: 124:106679

TITLE: Thiazolidinedione derivatives and related

antihyperglycemic agents in the treatment of impaired glucose tolerance to prevent or delay the onset of

noninsulin-dependent diabetes mellitus

INVENTOR(S): Olefsky, Jerrold; Antonucci, Tammy; Lockwood, Dean;

Norris, Rebecca

PATENT ASSIGNEE(S): Sankyo Co., Ltd., Japan

SOURCE: U.S., 15 pp. Cont.-in-part of U.S. Ser. No. 122,251,

abandoned.

CODEN: USXXAM

DOCUMENT TYPE:

Patent English

LANGUAGE: Engl:

FAMILY ACC. NUM. COUNT: 7

PATENT NO.	KIND DATE	APPLICATION NO.	DATE
US 5478852	A 19951226	US 1994-293899	19940823
US 5478852	C1 20010313		
WO 9507697	A2 19950323	WO 1994-US10187	19940909
WO 9507697	A3 19950511		•
W: AU, CA,	CN, CZ, FI, HU,	JP, KR, NO, NZ, RU, SK	
RW: AT, BE,	CH, DE, DK, ES,	FR, GB, GR, IE, IT, LU,	MC, NL, PT, SE
WO 9507694	A1 19950323	WO 1994-US10389	19940914
W: AU, CA,	CN, CZ, FI, HU,	JP, KR, MW, NO, NZ, RU	
RW: AT, BE,	CH, DE, DK, ES,	FR, GB, GR, IE, IT, LU,	MC, NL, PT, SE
AU 9478351	A1 19950403	AU 1994-78351	19940914

AU 679572	В2	19970703								
EP 719140	A1	19960703		EP	1994-92920	4	19940914			
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CN 1134669	A	19961030			1994-19405		19940914			
JP 09502727	T2	19970318		JP	1995-50933	3	19940914			
JP 3081245	B2	20000828								
HU 75874	A2	19970528		HU	1996-653		19940914			
CZ 283207	B6	19980114		CZ	1996-2822		19940914			
CZ 283208	B6	19980114			1996-2823		19940914			
CZ 283339	В6	19980318			1996-793		19940914			
JP 2000239167	A2	20000905		JP	2000-71978		19940914			
JP 2000273043	A2	20001003		JP	2000-71977	Ī	19940914			
NO 9601041	A	19960514		NO	1996-1041		19960314			
FI 9601213	A	19960514		FI	1996-1213		19960315			
AU 9717709	A1	19970529		AU	1997-17709)	19970403			
ĀU 706947	В2	19990701								
AU 9717710	A1	19970529		AU	1997-17710)	19970403			
AU 9952576	A1	19991202		AU	1999-52576	5	19991001			
AU 749416	B2	20020627								
NO 2000002963	Α	20000609			2000-2963		20000609			
NO 2000002964	Α	20000609			2000-2964		20000609			
PRIORITY APPLN. INFO.	:				93-122251	В2	19930915			
					94-292585	Α				
					94-293899		19940823			
					94-509333		19940914			
					95-509333		19940914			
					94-US10389		19940914			
				AU 19:	97-17709	А3	19970403			

OTHER SOURCE(S):

MARPAT 124:106679

AB Novel methods of using thiazolidinone derivs. and related antihyperglycemic agents to treat populations experiencing impaired glucose tolerance in order to prevent or delay the onset of noninsulin-dependent diabetes mellitus and complications arising therefrom, are disclosed. Effects of (+)-5-[[4-[(3,4-dihydro-6-hydroxy-2,5,7,8-tetramethyl-2H-1-benzopyran-2-yl)methoxy]phenyl]methyl]-2,4-thiazolidinedione (troglitazone) was clin. tested with patients with impaired glucose tolerance by the WHO criteria; the results showed that treatment with troglitazone correlated to redn. of fasting insulin levels and return of glucose tolerance to the normal range for ~70% of the subjects.

IT 122320-73-4

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(thiazolidinedione derivs. in prevention of onset of noninsulin-dependent diabetes)

RN 122320-73-4 HCAPLUS

CN 2,4-Thiazolidinedione, 5-[[4-[2-(methyl-2-pyridinylamino)ethoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

PAGE 2-A

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(FILE 'HOME' ENTERED AT 20:08:06 ON 03 OCT 2002)

FILE 'REGISTRY' ENTERED AT 20:08:18 ON 03 OCT 2002 STRUCTURE UPLOADED

L2 2 S L1

L3 48 S L1 FULL

FILE 'HCAPLUS' ENTERED AT 20:14:30 ON 03 OCT 2002

L4 490 S L3

L5 324 S L3/THU

L6 92 S L5 AND METHOD L7 56 S L6 AND DIAB?

L8 44 S L7 AND MELLIT?

L9 17 S L8 AND PD < MAY 20 1999

=> s 13 and polymo?

490 L3

127960 POLYMO?

L10 7 L3 AND POLYMO?

=> s 110 and blackler, p?/au

11 BLACKLER, P?/AU

L11 3 L10 AND BLACKLER, P?/AU

=> d ll1, ibib abs fhitstr, 1-3

L11 ANSWER 1 OF 3 HCAPLUS COPYRIGHT 2002 ACS



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2000:772629 HCAPLUS
ACCESSION NUMBER:
                                             133:340315
DOCUMENT NUMBER:
                                             Therapeutic action and properties of a polymorphic
TITLE:
                                             form of 5-[4-[2-(N-methyl-N-(2-
                                             pyridyl)amino)ethoxy]benzyl]thiazolidine-2,4-dione,
                                             maleic acid salt
                                             Blackler, Paul David James; Browne, Christine Marie;
INVENTOR(S):
                                             Coakley, Timothy G.; Giles, Robert Gordon; Morrissey,
                                             Gillian
PATENT ASSIGNEE(S):
                                              SmithKline Beecham PLC, UK; SmithKline Beecham (Cork)
                                             Limited
SOURCE:
                                              PCT Int. Appl., 21 pp.
                                             CODEN: PIXXD2
DOCUMENT TYPE:
                                              Patent
LANGUAGE:
                                              English
FAMILY ACC. NUM. COUNT:
PATENT INFORMATION:
         PATENT NO.
                                                                              APPLICATION NO. DATE
                                       KIND DATE
                                                  _____
                                                                              _____
         WO 2000-GB1520
                                                                                                              20000419
         WO 2000064896
                                        Α1
                                                   20001102
                W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU,
                       CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV,
                        MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG,
                        SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW,
                        AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
                RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
                                                                            EP 2000-920892
                                                                                                              20000419
                                         Α1
                                                  20020123
                       AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
                        IE, SI, LT, LV, FI, RO
         BR 2000009932
                                       Α
                                                   20020409
                                                                               BR 2000-9932
                                                                                                              20000419
         NO 2001005147
                                                   20011217
                                                                               NO 2001-5147
                                                                                                              20011022
                                         Α
                                                                                                        A 19990423
PRIORITY APPLN. INFO.:
                                                                          GB 1999-9473
                                                                          GB 1999-12196
                                                                                                        Α
                                                                                                              19990525
                                                                         WO 2000-GB1520
                                                                                                        W 20000419
AB
         A polymorphic form of 5-[4-[2-(N-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-
         pyridyl)amino)ethoxy]benzyl]thiazolidine-2, 4-dione, maleic acid salt (the
         "Polymorph") characterized in that it provides: (i) an IR spectrum
         contg. peaks at 1763, 912, 856 and 709 cm^{-1}; and/or (ii) a Raman spectrum
         contg. peaks at 1762, 1284, 912 and 888 cm^{-1}; and/or (iii) a solid-state
         13C NMR spectrum contg. peaks at 111.0, 113.6, 119.8, 129.1, 130.9, 131.8,
         134.7, 138.7, 146.5, 152.7, 157.5, 169.5, 171.0, 178.7 ppm; and/or (iv) an
         x-ray powder diffraction (XRPD) pattern which gives calcd. lattice
         spacings at 5.87, 5.30, 4.69, 4.09, 3.88, 3.61, 3.53 and 3.46 Angstroms; a
         process for prepg. such a compd., a pharmaceutical compn. contg. such a
         compd. and the use of such a compd. in medicine.
IT 155141-29-0
         RL: BAC (Biological activity or effector, except adverse); BSU (Biological
         study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL
         (Biological study); USES (Uses)
               (antidiabetic action and properties of polymorphic form of
               [[(N-methyl-N-(pyridyl)amino)ethoxy]benzyl]thiazolidinedione maleate)
RN
         155141-29-0 HCAPLUS
         2,4-Thiazolidinedione, 5-[[4-[2-(methyl-2-pyridinylamino)ethoxy]phenyl]met
CN
         hyl]-, (22)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)
         CM
         CRN
                  122320-73-4
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34 of 47 10/3/02 8:22 PM

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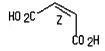
CMF



CM 2

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Double bond geometry as shown.



REFERENCE COUNT:

4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2002 ACS

Full Citing Text References

ACCESSION NUMBER: 2000:772627 HCAPLUS

DOCUMENT NUMBER: 133:340314

TITLE: Therapeutic action and properties of a polymorphic

form of 5-[4-[2-(N-methyl-N-(2-

pyridyl)amino)ethoxy]benzyl]thiazolidine-2,4-dione,

maleic acid salt

INVENTOR(S): Blackler, Paul David James; Giles, Robert Gordon;

Moore, Stephen; Sasse, Michael John

PATENT ASSIGNEE(S): SmithKline Beecham PLC, UK

SOURCE: PCT Int. Appl., 19 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1 PATENT INFORMATION:

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KIND DATE
                                                                                                                  APPLICATION NO. DATE
             PATENT NO.
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             WO 2000064893
                                                              A2
                                                                             20001102
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PRIORITY APPLN. INFO.:
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                                                                                                              GB 1999-12195
                                                                                                                                                            A 19990525
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                                                                                                                                                            W 20000419
             A polymorphic form of 5-[4-[2-(N-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-N-(2-methyl-
AΒ
             "Polymorph") characterized in that it provides: (i) an infra red
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pyridyl)amino)ethoxy]benzyl]thiazolidine-2,4-dione, maleic acid salt (the "Polymorph") characterized in that it provides: (i) an infra red spectrum contg. peaks at 1752, 1546, 1154, 621, and 602 cm⁻¹; and/or (ii) a Raman spectrum contg. peaks at 1751, 1243 and 602 cm⁻¹; and/or (iii) a solid-state NMR spectrum contg. peaks at 111.9, 114.8, 119.6, 129.2, 134.0, 138.0, 144.7, 153.2, 157.1, 170.7, 172.0 and 175.0 ppm; and/or (iv) an x-ray powder diffraction (XRPD) pattern which gives calcd. lattice spacings of 6.46, 5.39, 4.83, 4.68, 3.71, 3.63, 3.58, and 3.48 Angstroms; a process for prepg. such a compd., a pharmaceutical compn. contg. such a compd. and the use of such a compd. in medicine.

IT 168553-12-6

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(antidiabetic action of polymorphic form of

[[(N-methyl-N-(pyridyl)amino)ethoxy]benzyl]thiazolidinedione maleate)

RN 168553-12-6 HCAPLUS

CN 2,4-Thiazolidinedione, 5-[[4-[2-(methyl-2-pyridinylamino)ethoxy]phenyl]methyl]-, (2Z)-2-butenedioate (9CI) (CA INDEX NAME)

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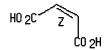
CRN 122320-73-4 CMF C18 H19 N3 O3 S



CM 2

CRN <u>110-16-7</u> CMF <u>C4 H4 O4</u>

Double bond geometry as shown.



L11 ANSWER 3 OF 3 HCAPLUS COPYRIGHT 2002 ACS

Full Citing Text References

ACCESSION NUMBER:

2000:772626 HCAPLUS

DOCUMENT NUMBER:

133:340313

TITLE:

Therapeutic action and properties of a polymorphic

form of 5-[4-[2-(N-methyl-N-(2-

pyridyl)amino)ethoxy]benzyl]thiazolidine-2,4-dione,

maleic acid salt

INVENTOR(S):

Blackler, Paul David James; Giles, Robert Gordon;

Sasse, Michael John

PATENT ASSIGNEE(S):

SmithKline Beecham P.L.C., UK

SOURCE:

PCT Int. Appl., 18 pp. CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

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PRIORITY APPLN. INFO.:
                                        GB 1999-9472
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                                        GB 1999-12197
                                                        A 19990525
                                       WO 2000-GB1514
                                                        W 20000419
AΒ
    A polymorphic form of 5-[4-[2-(N-methyl-N-(2-
    pyridyl)amino)ethoxy]benzyl]thiazolidine-2,4-dione, maleic acid salt (the
     "Polymorph") characterized in that it: (i) provides an IR spectrum
     contg. peaks at 1360, 1326, 1241, 714 and 669 cm^{-1}; and/or (ii) provides a
     Raman spectrum contg. peaks at 1581, 768, 670, 271 and 226 cm^{-1}; and/or
     (iii) provides a solid-state NMR spectrum contg. peaks at chem. shifts
     substantially; and/or (iv) provides an x-ray powder diffraction (XRPD)
     pattern contg. peaks; a process for prepg. such a compd., a pharmaceutical
     compn. contq. such a compd. and the use of such a compd. in medicine.
IT 168553-12-6
    RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL
```

(Biological study); USES (Uses)

(antidiabetic action of polymorphic form of

[{(N-methyl-N-(pyridyl)amino)ethoxy]benzyl]thiazolidinedione maleate) 168553-12-6 HCAPLUS

2,4-Thiazolidinedione, 5-[[4-[2-(methyl-2-pyridinylamino)ethoxy]phenyl]met hyl]-, (2Z)-2-butenedioate (9CI) (CA INDEX NAME)

CM 1

RN CN

> CRN 122320-73-4 CMF C18 H19 N3 O3 S

CM 2

CRN 110-16-7 CMF C4 H4 O4

Double bond geometry as shown.

=> d his

(FILE 'HOME' ENTERED AT 20:08:06 ON 03 OCT 2002)

FILE 'REGISTRY' ENTERED AT 20:08:18 ON 03 OCT 2002
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L2 2 S L1
L3 48 S L1 FULL

FILE 'HCAPLUS' ENTERED AT 20:14:30 ON 03 OCT 2002

L4 490 S L3 L5 324 S L3/THU

L6 92 S L5 AND METHOD L7 56 S L6 AND DIAB? L8 44 S L7 AND MELLIT?

L9 17 S L8 AND PD < MAY 20 1999

L10 7 S L3 AND POLYMO?

L11 3 S L10 AND BLACKLER, P?/AU

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L12 4 L10 NOT L11

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L12 ANSWER 1 OF 4 HCAPLUS COPYRIGHT 2002 ACS

Full Citing Text References

ACCESSION NUMBER: 2002:504785 HCAPLUS

DOCUMENT NUMBER: 137:83621

TITLE: Preparation and use of 5-[4-[2-(N-methyl-N-(2-

pyridyl)amino)ethoxy]benzyl]thiazolidine-2,4-dione

methanesulfonate

INVENTOR(S): Craig, Andrew Simon; Ho, Tim Chien Ting; Millan,

Michael; O'Keeffe, Deirdre

PATENT ASSIGNEE(S): Smithkline Beecham P.L.C., UK

SOURCE: PCT Int. Appl., 41 pp.

CODEN: PIXXD2
DOCUMENT TYPE: Patent

LANGUAGE: Facence English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PAS	PATENT NO.			KI	KIND DATE			APPLICATION NO. DATE										
WO	2002051839			A1 20020704			WO 2001-GB5751				20011221							
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						FΙ,												
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PRIORIT	RIORITY APPLN. INFO							GB 2000-31521										
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									GB 2	<u> </u>	3152	<u>8</u>	Α	2000	1222			

GΙ

$$0 = \begin{cases} 1 & \text{if } 1 \\ 1 & \text{if } 1 \end{cases}$$

AB A compd. 5-[4-[2-(N-methyl-N-(2-pyridyl)amino)ethoxy]benzyl]thiazolidine-2,4-dione (I) methanesulfonate salt (II) or solvate thereof; a process for prepg. I, a compn. comprising I and its therapeutic use is disclosed. Four polymorphic forms were prepd. and characterized. For instance, MsOH (0.54 mL) was added to a mixt. of I (3.0 g) in EtOAc (60 mL) and was heated with agitation to reflux to give a suspension. The resulting mixt. was cooled to 21°C, the solid formed collected by filtration, washed with EtOAc and dried under vacuum for 16 h (3.73 g yield). Polymorphic forms I-IV were characterized by at least one of the following means: aq. soly., m.p., 1H-NMR (soln.), 13C-NMR (solid state), IR/Raman spectra, XRPD and DSC. II is a stable solid with good water soly., desirable flow properties and is amenable to large scale processing (milling). II is useful for the prevention/treatment of diabetes mellitus.

IT 439902-56-4P

RL: IMF (Industrial manufacture); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(polymorphic forms I-IV characterized; prepn. and characterization of 5-[4-[2-(N-Me-N-(2-pyridyl)amino)ethoxy]benzyl]thia zolidine-2,4-dione methanesulfonate)

RN 439902-56-4 HCAPLUS

CN 2,4-Thiazolidinedione, 5-[[4-[2-(methyl-2-pyridinylamino)ethoxy]phenyl]methyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

CM 1

CRN 122320-73-4 CMF C18 H19 N3 O3 S

PAGE 1-A

PAGE 2-A

CM 2

CRN <u>75-75-2</u> CMF C H4 O3 S

REFERENCE COUNT:

THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 2 OF 4 HCAPLUS COPYRIGHT 2002 ACS

2

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Full Citing
Text References
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ACCESSION NUMBER: 2002:256258 HCAPLUS

DOCUMENT NUMBER: 136:299688

TITLE: Novel polymorphic forms of 5-[4-[2-[N-methyl-N-(2-

pyridyl)amino]ethoxy]benzyl] thiazolidine-2,4-dione

maleate and process for their preparation

INVENTOR(S): Chebiyyam, Prabhakar; Mamillapalli, Ramabhadra Sarma;

Krishnamurthi, Vyas; Seella, Vishnuvardhan Reddy;

Gaddam, Om Reddy

PATENT ASSIGNEE(S): Reddy's Research Foundation, India; Cord, Janet I.

SOURCE: PCT Int. Appl., 40 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

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PATENT NO.
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                           DATE
                                           APPLICATION NO. DATE
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     WO 2002026737
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                            20020404
                                           WO 2001-US29896 20010925
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             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL,
             PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG,
             US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
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             DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
             BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
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                            20020408
                                           AU 2001-91232
                                                            20010925
PRIORITY APPLN. INFO.:
                                        IN 2000-MA805
                                                         A 20000926
                                        WO 2001-US29896 W 20010925
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This invention relates to novel **polymorphic**/pseudopolymorphic forms of 5-[4-[2[N-methyl-N-(2-pyridyl)amino]ethoxy]benzyl] thiazolidine-2,4-dione maleate (I). The invention also relates to a pharmaceutical compn. comprising the novel **polymorphic** form or their mixt. and a pharmaceutically acceptable carrier. The **polymorphic** forms of the present invention are more active, as antidiabetic agent, than the hitherto known 5-[4-[2-[N-2-methyl-N-(2-pyridyl)amino]ethoxy]benzyl] thiazolidine-2,4-dione maleate. I was dissolved in ethanol and was allowed to cool to room temp. over a period of 18 h to yield 80% of >99% pure **polymorphic** form of I.

IT 155141-29-0P

RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (novel **polymorphic** forms of triazolidinedione maleate and process for their prepn.)

RN 155141-29-0 HCAPLUS

CN 2,4-Thiazolidinedione, 5-[[4-[2-(methyl-2-pyridinylamino)ethoxy]phenyl]met hyl]-, (2Z)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

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CRN 122320-73-4 CMF C18 H19 N3 O3 S

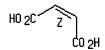
42 of 47 10/3/02 8:22 PM



CM 2

CRN 110-16-7 CMF C4 H4 O4

Double bond geometry as shown.



REFERENCE COUNT:

6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 3 OF 4 HCAPLUS COPYRIGHT 2002 ACS

Full Citing Text References

ACCESSION NUMBER: 2001:724803 HCAPLUS

DOCUMENT NUMBER: 136:79548

TITLE: Inhibition of RXR and PPARy ameliorates diet-induced obesity and type 2 diabetes

AUTHOR(S): Yamauchi, Toshimasa; Waki, Hironori; Kamon, Junji;

Murakami, Koji; Motojima, Kiyoto; Komeda, Kajuro;

Miki, Hiroshi; Kubota, Naoto; Terauchi, Yasuo; Tsuchida, Atsuko; Tsuboyama-Kasaoka, Nobuyo; Yamauchi, Naoko; Ide, Tomohiro; Hori, Wataru; Kato, Shigeaki;

Naoko; Ide, Tomohiro; Hori, Wataru; Kato, Shigeaki; Fukayama, Masashi; Akanuma, Yasuo; Ezaki, Osamu; Itai, Akiko; Nagai, Ryozo; Kimura, Satoshi; Tobe, Kazuyuki; Kagechika, Hiroyuki; Shudo, Koichi; Kadowaki, Takashi Department of Internal Medicine, Graduate School of

CORPORATE SOURCE: Department of Internal Medicine, Graduate School of Medicine, University of Tokyo, Tokyo, 113-8655, Japan

SOURCE: Journal of Clinical Investigation (2001), 108(7),

1001-1013

CODEN: JCINAO; ISSN: 0021-9738

PUBLISHER: American Society for Clinical Investigation

DOCUMENT TYPE: Journal LANGUAGE: English

PPARy is a ligand-activated transcription factor and functions as a heterodimer with a retinoid X receptor (RXR). Supraphysiol. activation of PPARy by thiazolidinediones can reduce insulin resistance and hyperglycemia in type 2 diabetes, but these drugs can also cause wt. gain. Quite unexpectedly, a moderate redn. of PPARy activity obsd. in heterozygous PPARy-deficient mice or the Prol2Ala polymorphism in human PPARy, has been shown to prevent insulin resistance and obesity induced by a high-fat diet. In this study, we investigated whether functional antagonism toward PPARy/RXR could be used to treat obesity and type 2 diabetes. We show herein that an RXR antagonist and a PPARy antagonist decrease triglyceride (TG) content in white adipose tissue, skeletal muscle, and liver. These inhibitors potentiated leptin's effects and increased fatty acid combustion and energy dissipation, thereby ameliorating HF diet-induced obesity and insulin Paradoxically, treatment of heterozygous PPARyresistance. deficient mice with an RXR antagonist or a PPARy antagonist depletes white adipose tissue and markedly decreases leptin levels and energy dissipation, which increases TG content in skeletal muscle and the liver, thereby leading to the re-emergence of insulin resistance. Our data suggested that appropriate functional antagonism of PPARy/RXR may be a logical approach to protection against obesity and related diseases such as type 2 diabetes.

IT **122320-73-4**, Rosiglitazone

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(inhibition of RXR and PPAR γ ameliorates diet-induced obesity and type 2 diabetes)

RN 122320-73-4 HCAPLUS

CN 2,4-Thiazolidinedione, 5-[[4-[2-(methyl-2-pyridinylamino)ethoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



REFERENCE COUNT:

55

THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

ANSWER 4 OF 4 HCAPLUS COPYRIGHT 2002 ACS

Citing Full References Text

ACCESSION NUMBER:

1999:437778 HCAPLUS

DOCUMENT NUMBER:

131:197757

TITLE:

Loss-of-function mutations in PPARy associated

with human colon cancer

AUTHOR(S):

Sarraf, Pasha; Mueller, Elisabetta; Smith, Wendy M.; Wright, Harold M.; Kum, Jennifer B.; Aaltonen, Lauri A.; De la Chapelle, Albert; Spiegelman, Bruce M.; Eng,

Charis

CORPORATE SOURCE:

Department of Cancer Biology Dana-Farber Cancer

Institute Department of Cell Biology, Harvard Medical

School, Boston, MA, 02115, USA

SOURCE:

Molecular Cell (1999), 3(6), 799-804

CODEN: MOCEFL; ISSN: 1097-2765

PUBLISHER: DOCUMENT TYPE: Cell Press Journal English

LANGUAGE:

The gamma isoform of the peroxisome proliferator-activated receptor, PPARy, regulates adipocyte differentiation and has recently been shown to be expressed in neoplasia of the colon and other tissues. The authors have found four somatic PPARy mutations among 55 sporadic colon cancers: one nonsense, one frameshift, and two missense mutations. Each greatly impaired the function of the protein. C.472delA results in deletion of the entire ligand binding domain. Q286P and K319X retain a total or partial ligand binding domain but lose the ability to activate transcription through a failure to bind to ligands. R288H showed a normal response to synthetic ligands but greatly decreased transcription and binding when exposed to natural ligands. These data indicate that colon cancer in humans is assocd. with loss-of-function mutations in PPARy.

IT 122320-73-4, BRL 49653

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)

(loss-of-function mutated PPARy assocd. with human colon cancer binding of and transactivation response to)

122320-73-4 HCAPLUS RN

2,4-Thiazolidinedione, 5-[[4-[2-(methyl-2-pyridinylamino)ethoxy]phenyl]met CN hyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

REFERENCE COUNT:

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L8
             17 S L8 AND PD < MAY 20 1999
L9
              7 S L3 AND POLYMO?
L10
              3 S L10 AND BLACKLER, P?/AU
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L12
              4 S L10 NOT L11
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L13
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ring nodes:
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Chain bonds:
    7-10 7-11 11-12 12-14 14-17 20-23 23-24 24-27 25-31 28-30

ring bonds:
    1-2 1-6 2-3 3-4 4-5 5-6 15-16 15-20 16-17 17-18 18-19 19-20 25-26 25-29 26-27 27-28 28-29

exact/norm bonds:
    7-10 12-14 14-17 25-29 25-31 28-29 28-30

exact bonds:
    7-11 11-12 20-23 23-24 24-27 25-26 26-27 27-28

normalized bonds:
    1-2 1-6 2-3 3-4 4-5 5-6 15-16 15-20 16-17 17-18 18-19 19-20

isolated ring systems:
    containing 1: 15: 25:
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G1:CH3,Et

G2:0,S

Match level:
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:CLASS 10:CLASS 11:CLASS 12:CLASS 14:CLASS 15:Atom 16:Atom 17:Atom 18:Atom 19:Atom 20:Atom 23:CLASS 24:CLASS 25:Atom 26:Atom 27:Atom 28:Atom 29:Atom 30:CLASS 31:CLASS